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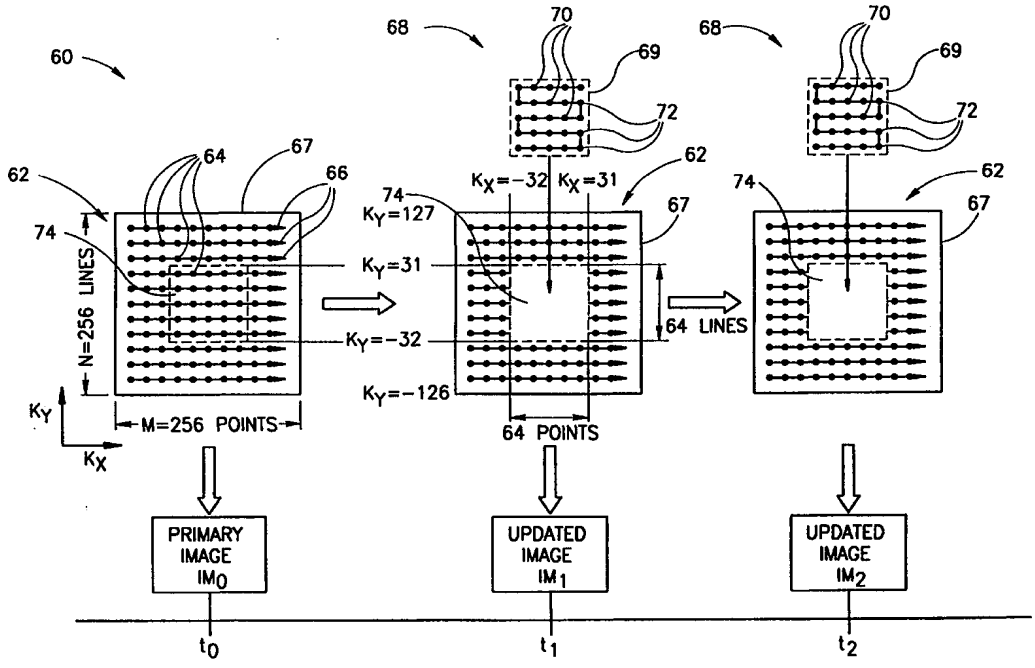

(57) **Abstract**

A method is provided for rapidly producing high resolution two–dimensional and three–dimensional real–time images of an object by MRI imaging comprising, acquiring a set of data for the object at a raster of coordinate points in a region in a k–space using a first MRI imaging technique and updating some of the data using a second MRI imaging technique.

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KEYHOLE MRI

FIELD OF THE INVENTION

The invention relates to magnetic resonance imaging techniques and in particular to magnetic resonance imaging techniques for rapidly producing high resolution two dimensional and three dimensional real time images.

BACKGROUND OF THE INVENTION

Magnetic resonance imaging, "MRI" is an important noninvasive methods for looking into the human body. Medical MRI scanners first became available in the early 1980s and since then MRI equipment and methodology has advanced rapidly. Today, conventional MRI scanners are capable of imaging internal body structures and resolving details smaller than a cubic millimeter in size and MRI scanners with microscopic resolution a thousand times better (0.1 mm cube) are available.

MRI is based on the phenomenon that when a sample material, including human tissue, is introduced into a magnetic field B, nuclei in the sample having intrinsic spin will precess around the direction of B with a component of spin parallel or anti-parallel to B. This is because nuclei with spin behave in many ways like small dipole magnets that spin around their own axes. The precession frequency about the magnetic field is known as the Larmor frequency. The relationship between the nuclear spin, $\vec{S}$, and the magnetic moment, $\vec{\mu}$, of a nucleus is $\vec{\mu} = \gamma * \vec{S}$ where the proportionality constant, γ, is the gyromagnetic ratio of the nucleus, which is distinctive for each nucleus. The Larmor frequency, ω, with which the spin and associated magnetic moment of the nucleus precess around the magnetic field is equal to γB.

Slightly more of the nuclei are aligned with components of spin parallel to the direction of B than are aligned anti-parallel to B because nuclei aligned with B are in a lower energy state than nuclei aligned against B. The material is therefore polarized with a net spin density per unit volume, $\rho(x,y,z)$, and a magnetization density per unit volume, $m(x,y,z) = \gamma * \rho(x,y,z)$, pointing in the direction of B.

The gyromagnetic ratios for some common nuclei are: ^{1}H, 4257 Hz/gauss; ^{13}C, 1070 Hz/gauss; ^{23}Na, 3368. In a 1.5 Tesla polarizing B field these gyromagnetic ratios result in precession frequencies of 63.85 MHz, 16.05MHz, and 50.51MHz respectively. For a given polarizing B field, however, the observed Larmor frequency for a particular nucleus is shifted from the expected value γB and depends upon the molecule in which the nucleus is found and

how the nucleus is bonded in the molecule. The shift is caused by currents that are induced in the electron cloud of the molecule by B that shield the nucleus from B. The magnitude of the shift is substantially proportional to B and can be used to identify the chemical environment in which the nucleus is found. This shift is called a chemical shift.

The Larmor frequencies of nuclei, because they can be used to identify the chemical environment in which nuclei are found and because they are dependent on the polarizing magnetic field B, can be used to effectively map the density distributions of nuclei and molecules in an object. If the densities of the nuclei and molecules vary with different internal structures of the object then these internal structures can be identified and imaged.

The basic approach to using Larmor frequencies for imaging an object is to produce a magnetic field that changes over the volume of the object so that the Larmor frequencies of nuclei investigated vary as a function of position. The nuclei are then stimulated to radiate energy at their Larmor frequencies. The signal intensity at a particular frequency is proportional to the number of radiating nuclei at the position in the object which is identified by the signal frequency. As a result, mappings of the densities of various nuclei in the object can be made which are functions of position in the object and internal structures of the object can be visualized.

Implementing the above procedure is generally performed by polarizing the object with a strong homogeneous magnetic field, B_0, in the z direction. B_0 polarizes (along the z axis), all nuclei having spin and magnetic moment, and each type of nucleus precesses around B_0 with its own Larmor frequency. An imaging nucleus, *i.e.* nucleus whose density it is desired to image having a gyromagnetic ratio γ and Larmor frequency $\omega_0=\gamma B_0$, is selected for imaging by rotating its spin density $\rho(x,y,z)$ and associated magnetization density $m(x,y,z)$ away from the z axis. This produces a net spin density and magnetization density perpendicular to z which rotate with Larmor frequency ω_0. The rotation is achieved by applying an RF selection pulse, having a narrow frequency spectrum centered at the Larmor frequency ω_0 of the imaging nucleus and magnetic field B_{Sx} along the x axis, for a short period of time T_S. B_{Sx} causes the net spin density of the imaging nucleus to rotate away from the z axis by an angle $\gamma B_{Sx} T_S$, conventionally called the flip angle. A receiver coil positioned at the side of the object with the plane of the coil parallel to the z axis (*i.e.* the perpendicular to the plane of the coil is perpendicular to the z axis) senses the rotating magnetic field moving with the rotating magnetization density. The rotating magnetic field illuminates the receiver ω_0 times a second, generating a signal, SIG(t), in the coil, which oscillates with frequency ω_0.

Gradient fields in the z direction, which vary linearly with x, y and z, are then applied to the object. The gradient fields cause the frequency of rotation of the magnetization density to vary around Larmor frequency ω_0 as a function of position in the object. If G_x, G_y, and G_z are the derivatives of the gradient fields, the signal becomes, to within a constant: $SIG(t)= \iiint \rho(x,y,z) \exp[i\gamma(B_0+G_x x+G_y y+G_z z)t]\, dxdydz = \exp[i\omega_0 t]S(t)$. S(t) is the position dependent part of the integral, it has been assumed that the angle of rotation of $\rho(x,y,z)$ away from the z axis is $\pi/2$, and relaxation of the spin density to zero in the transverse plane and to equilibrium along the z axis is ignored.

By changing variables so that $k_x= (\gamma G_x x)t$, $k_y= (\gamma G_y y)t$ and $k_z= (\gamma G_z z)t$, S(t) can be written as a function of position in a "k-space". $S(t)\rightarrow S(k_x,k_y,k_z)= S(\vec{k})$, and:

$$S(\vec{k})= \iiint \rho(x,y,z) \exp[i\,(k_x x+k_y y+k_z z)]\, dxdydz = \iiint \rho(\vec{r}) \exp[i\,\vec{k}\cdot\vec{r}\,]d^3r.$$

The last integral is the Fourier transform of the spin density function $\rho(x,y,z)$ of the imaging nucleus. $S(\vec{k})$ is a "k-transform" of $\rho(x,y,z)$ and $\vec{k}$ and $\vec{r}$ are conjugate variables so that $\rho(\vec{r}) = \iiint S(\vec{k}) \exp[i\,\vec{k}\cdot\vec{r}\,]d^3k$.

When the imaging nuclei are first flipped away from the z axis they precess together coherently with a net spin density and magnetization density in the xy plane. With time, however, the coherence in the transverse xy plane decays to zero and the spin density relaxes to the equilibrium state where the imaging nuclei are polarized along the z axis. The decay of net transverse spin density and return to equilibrium along the z axis are characterized by different time constants known as T_2 and T_1 respectively. When inhomogenities in the magnetic field are present the decay of transverse spin density is accelerated and is characterized by a time constant known as T_2^*. The relaxation times are related by the inequality $T_2^* < T_2 < T_1$.

The various relaxation times of imaging nuclei are quite sensitive to the chemical environment of the imaging nuclei and the molecular structure of the molecules in which they are bound. This sensitivity allows different materials to be discriminated from each other by the rate at which their MRI signals decay. In particular in medical and biological imaging different tissues and features in biological tissues can be identified and contrast enhanced by manipulating their T_1, T_2 and T_2^* time constants. T_2^* for example is of particular interest in functional neuroimaging.

Often the three dimensional imaging problem is reduced to a two dimensional one by selecting nuclei for imaging that are confined to a thin transverse "xy" slice of an object imaged. Assume that while the RF selection pulse is on, a selection gradient field that varies

linearly with z with a gradient G_{SZ} is applied to the object parallel to the z axis. The Larmor frequency of the imaging nuclei selected will then be shifted from ω_0 as a function of position along the z axis by an amount $\gamma G_{SZ}z$. If the RF selection pulse is a narrow pulse with a central frequency ω_S, only those imaging nuclei in a thin transverse slice at z coordinate Z_S such that $\omega_S = \omega_0 + \gamma G_Z Z_S$ will be rotated away from the z axis by the RF selection pulse. By acquiring data for two dimensional k-functions, $S(k_X,k_Y,Z_S)$, for a range of values Z_S, a three dimensional image of the object can be constructed.

Many different techniques and procedures have been developed for MRI imaging. All involve procedures for evaluating the k-transform, $S(\vec{k})$, of an object at many points in a raster of points in k-space so that the Fourier transform of $S(\vec{k})$ results in a proper evaluation of $\rho(\vec{r})$.

Typical MRI imaging techniques are the conventional gradient echo (GE) and spin echo (SE) imaging sequences. Each of these sequences acquire k-transform data for a slice of an object imaged at points in k-space (hereafter "read points") along lines in k-space (hereafter "read lines") parallel to the k_X axis. The sequences begin with an RF slice selection pulse and acquire data for only a single read line each time they are run. To acquire data for a complete slice of the object the sequences are repeated as many times as necessary to read data along all the read lines required for the k-transform of the slice. The sequences are similar except that the SE sequence includes a focusing or rephasing RF pulse for neutralizing phase differences in the spins of imaging nuclei arising from magnetic field inhomogenities.

GE and SE sequences can be used to acquire high resolution k-transforms using moderate gradient fields and receiver bandwidths. However, acquiring data using these sequences is relatively slow. Delay times between repetitions, T_R, of both these sequences are generally long. T_R depends upon, among other factors, how fast the spin density which is rotated away from the polarizing field recovers its equilibrium value along the polarizing field direction after a repetition of the sequence. T_R must therefore be longer than the time, T_1, which is characteristic of the recovery if repeated sequences are all to have the substantially the same signal strength.

In most plant and animal tissue, T_1 ranges from 0.2 to 1 sec. Therefore, conventional GE and SE sequences are inherently slow, with total image times for a slice ranging from seconds to minutes. However, their long imaging times restrict their use in real time rapid imaging of motion of internal organs and metabolic changes in the human body.

Real time imaging of physiological processes such as cardiac contractility, peristalsis and brain activity are important areas of medical research. MRI techniques are needed for high resolution rapid imaging for these and other dynamic biological processes. However, even the most basic of the body's internal movements and metabolic changes requires imaging techniques that can produce clear accurate pictures in tenths of a second. For example, the heart beats with a frequency on the order of one beat per second. To follow the progress of a single heartbeat, or assess an arrhythmic event, it would be advantageous to acquire high definition images of the heart on the order of every 0.1 seconds or less.

Techniques exist for fast temporal MRI imaging. One such technique is echo planar imaging (EPI). In EPI, all or a large part of the area of k-space of a slice to be imaged is scanned in a short period of time following a single RF slice selection pulse. Data for imaging a complete slice of an object using EPI can be accumulated in a time period of from 20 to 100 milliseconds. While these time frames are useable for imaging physiological processes, the images obtained with EPI are generally inferior in resolution to images produced using conventional GE and SE techniques.

Fast EPI techniques also require special hardware and large receiver band widths and they use very strong rapidly changing gradient fields. The rapidly changing fields can produce undesirable biological effects, such as electrical stimulation of nerves and slight torques on cones in the retina which are evidenced by light flashes in the eye.

Fig. 1A shows an EPI sequence 20, for acquiring with one repetition of EPI sequence 20, a two dimensional k-transform, $S(k_X,k_Y,Z_S)$, (hereafter, $S(k_X,k_Y)$) for a complete slice of an object at N x M read points. An RF slice selection pulse 24 and a selection gradient field 22 and 26 are applied to the body being imaged to select a slice to be imaged at a z coordinate Z_S. Data is taken using a phase encoding gradient 28, comprising N-1 phase blips 36, and a read gradient 32, comprising N read blips 38, of constant magnitude and alternating sign. Read blips 38 are T_M seconds long.

Phase encoding gradient field 28 begins with a negative gradient 30, which dephases the spins and sets k_Y to a minimum negative value. This minimum negative value is the k_Y coordinate of a first read line of M points in k-space at which data is sampled. A read gradient field 32, begins with a negative gradient 34, which dephases the spins and sets k_X to a minimum negative value which is the k_X coordinate of the left most point of each read line in k-space. Following gradients 30 and 34, read gradient 32 progresses with N read gradient blips 38 during which data for $S(\vec{k})$ is recorded . At the end of each read gradient blip 38 a phase gradient blip 36 increases k_Y by a constant amount. Phase blips 36 and read blips 38 are

carefully timed so that the centers of phase blips 36 occur at the zero crossover points between positive and negative read blips 38. This timing ensures that each read line in k-space begins and ends with the same k_X coordinates as the other read lines in k-space.

A data signal 40, comprises a pulse train of N data echo pulses 42, one for each read blip 38. Each data echo pulse 42 is substantially centered on a read blip 38, and is sampled M times, usually at equal time intervals, during the duration T_M of each read blip 38. Therefore, with each read blip 38, a set of M data values for $S(\vec{k})$ is acquired at M equally spaced points on a read line in k-space, parallel to the k_X axis. EPI sequence 20 therefore records in one repetition N x M data values for $S(\vec{k})$ in a total imaging time for the slice $T_I = N \times T_M$ seconds.

A sampling trajectory 50 in k-space, traversed by using EPI sequence 20 for sampling data at N x M points 51, is shown in Fig. 1B. Trajectory 50 is a series of equally spaced read lines 52, parallel to the k_X axis connected by short phase lines 54, parallel to the k_Y axis. The length of phase lines 54 is equal to the time integral of a phase blip 36, multiplied by the gyromagnetic ratio of an imaging nucleus whose density distribution is imaged. The length of read lines 52 is equal to the time integral of a read blip 38, multiplied by the gyromagnetic ratio of the imaging nucleus. Phase gradient 30 and read gradient 34, displace the beginning of trajectory 50 to point 56. Arrows 58, indicate the direction of traversal along trajectory 50 as data is sequentially taken at points 51 on trajectory 50.

For rapid, snapshot imaging of motions and processes in the human body, conventional MRI imaging techniques have generally satisfactory resolution but are too slow. Fast techniques, such as EPI, are rapid enough, but lack resolution and have serious technical risks and drawbacks.

It would be desirable to have an imaging technique that would have the resolution of conventional GE and SE techniques but produce images in time frames approaching that of fast EPI techniques.

It is further desirable that such imaging techniques not require pulsed gradient fields with time rates of change that might produce undesirable biological effects.

SUMMARY OF THE INVENTION

It is an object of one aspect of the present invention to provide an MRI method for two and three dimensional MRI imaging that can be used to produce a sequential series of high resolution images of an object in periods of time short enough so that the method can be used for rapid, real time imaging, of processes in the body and motion of body organs.

A preferred embodiment of the method comprises acquiring a high resolution primary MRI k-transform, $S_0(\vec{k})$, of an object at time t_0 and updating only some of its values while retaining the rest unchanged to produce sequential k-transforms of the object, $S_1(\vec{k})$, $S_2(\vec{k})$,... $S_n(\vec{k})$, at subsequent times $t_1, t_2 \ldots t_n$, as the object changes. By updating only some of the data for each sequential k-transform it is possible to produce the sequential k-transforms very rapidly. By using data from the high resolution primary k-transform in the sequential k-transforms, it is possible to substantially preserve the high resolution of the primary k-transform in the sequential k-transforms.

The values of $S_0(\vec{k})$ which are updated are, preferably, only those that change significantly with the changes in the object. Those values of $S_0(\vec{k})$ that do not change significantly with the changes in the object do not have to be updated and therefore are preferably retained from k-transform to k-transform. As a result, each of the k-transforms $S_n(\vec{k})$, at times subsequent to the acquisition of the primary k-transform, has substantially the same number of accurate data points as the primary k-transform $S_0(\vec{k})$. Therefore, the real space images of the object which are constructed from $S_1(\vec{k})$, $S_2(\vec{k})$,... $S_n(\vec{k})$ at times $t_1, t_2 \ldots t_n$ all have approximately the same spatial resolution as the primary real space image of the object.

The possibility of advantageously differentiating between values of $S_0(\vec{k})$ that change and values that substantially do not change with changes in an object imaged, is a result of the form of the dependence of $S_0(\vec{k})$ on $\vec{k}$. $S_0(\vec{k})$ generally changes significantly only for points $\vec{k}$ in a limited volume of k-space of size $1/L^3$, centered at the k-space origin, where L^3 is a real space volume characteristic of features of interest under observation in the object imaged. For points $\vec{k}$ outside k-space volume $1/L^3$, $S_0(\vec{k})$ does not change significantly.

This dependence of $S_0(\vec{k})$ on $\vec{k}$ can be understood from the relationship between the conjugate variables $\vec{k}$ and $\vec{r}$. Let R_X be the x axis spatial resolution of an image constructed from a k-transform $S(\vec{k})$ of the object. Let K_X be the range along the k_X axis over which data for $S(\vec{k})$ is accumulated. Then, from a well known characteristic of Fourier transforms, $K_X R_X \cong 1$. Therefore, if an MRI image of an object is required to have a resolution R, in all three dimensions (for simplicity it is assumed the resolution is the same along all three axes though there is no necessity for this to be so), the primary k-transform of the object, $S_0(\vec{k})$, is evaluated over a primary raster of points in k-space for which $-1/(2R) \leq |\vec{k}| \leq 1/(2R)$.

From similar considerations, objects, or features of an object, which have characteristic length of magnitude L, have significant values for $S_0(\vec{k})$ at points $\vec{k}$ for which, $|\vec{k}| \leq 1/(2L)$. For changes on the order of $\pm\Delta L$, large relative changes in the amplitude and phase of $S_0(\vec{k})$ occur in a bandwidth of $\vec{k}$ values for which $|\vec{k}|$ is in the region $k_0(1\pm\Delta L/L)$, where $k_0 = 1/L$, and it is assumed that L is significantly larger than ΔL. For $|\vec{k}| >> 1/[2(L-\Delta L)]$, essentially only the phase of $S_0(\vec{k})$ changes while the magnitude remains unchanged. A change in phase is equivalent to a displacement in real space. Neglecting these phase changes for large values of $|\vec{k}| \sim 1/R$ results in a potential error of $\sim 1/2R$ in the location of details of size 1/R in the real image of the object reconstructed from $S_0(\vec{k})$.

As a result, if changes of order $\pm\Delta L$ in an object or feature of characteristic length L are being observed over the course of a time study, it is generally sufficient to update $S_0(\vec{k})$, only for values of $\vec{k}$ for which $|\vec{k}| \leq 1/[2(L-\Delta L)]$ in order to follow the changes with spatial images having substantially the resolution R of the primary spatial image.

Therefore, in accordance with a preferred embodiment of the present invention, updates of $S_0(\vec{k})$ at times $t_1, t_2 \ldots t_n$ are preferably taken at a raster of points bounded in k-space by a cube having edges of length on the order of 1/L which is centered at the origin of k-space. Values of $S_0(\vec{k})$ at points in k-space outside this cube, are preferably retained from k-transform to k-transform.

The number of points at which updates of the primary k-transform $S_0(\vec{k})$ are made, in comparison to the number of data points in the primary image, can be approximated by the ratio of the k-space volume of the update raster of points to the k-space volume of the primary raster of points. This ratio is equal to R^2/L^2 and R^3/L^3 for two and three dimensional k-transforms respectively. It can be seen that even small ratios of R to L lead to very large reductions in the number of data points in an update compared to the number of data points in the primary k-transform $S_0(\vec{k})$.

Quite generally, for a feature in an object to be observed adequately, the resolution must be smaller than the feature and preferably significantly smaller than the feature (*i.e.* R<<L). The number of values of $S_0(\vec{k})$ which change significantly with changes in the features of the object under observation is therefore often much smaller than the total number of data points in $S_0(\vec{k})$. Updating can therefore generally be done very quickly in comparison to the acquisition time of the original primary k-transform $S_0(\vec{k})$.

This is not only because there are simply fewer data points to be evaluated for an update than for a primary image. The main advantage is that the reduced number of data points in the update permit the use of very fast MRI imaging techniques, such as for example EPI, to perform the updates. These techniques are not particularly attractive for rapid MRI imaging when used to acquire large amounts of data for a high resolution k-transform. When used to acquire data over large volumes of k-space they are expensive, require special equipment and very high, potentially harmful, gradient field time derivatives, and produce results with generally inadequate resolution. But they can be used to advantage for acquiring update data over a reduced number of data points. With the reduced number of data points these techniques can perform k-transform updates in time spans of from 20-120msec with the moderate field strengths and receiver bandwidths used in conventional GE and SE techniques.

It is thus seen that by sectioning k-space, in accordance with a preferred embodiment of the present invention, it is possible to use combinations of high resolution (for example, preferably, GE and SE sequences) and very fast MRI imaging techniques (for example, preferably, EPI sequences) to provide real time imaging of an object that is both very fast and very accurate. Furthermore this can be done without recourse to problematic gradient field derivatives or special equipment.

It is realized that different MRI imaging sequences, and not only those mentioned herein, can advantageously be used for acquiring data over k-space regions that are sectioned in accordance with a preferred embodiment of this invention. It is therefore possible to combine different MRI sequences in accordance with a preferred embodiment of the invention to provide MRI imaging techniques that are sensitive to different types of temporal changes in the body, such as motional changes due to peristalsis or cardiac contractility or physiological changes resulting from neural activity. For example in some preferred embodiments of the present invention, preferably, GE or SE MRI imaging sequences are used to acquire a high resolution primary k-transform of an object imaged and updates are performed using, preferably, a fast EPI sequence. Since EPI is inherently T_2^* sensitive, MRI methods in accordance with a preferred embodiment of the present invention, are particularly suitable for use with contrast agents such as Gd-DTPA in perfusion studies, and in functional neuroimaging using contrast agents or dependent upon changes in blood oxygenation. By incorporating 180 degree RF pulses in the MRI sequences the methods can be made T_2 sensitive instead of T_2^* sensitive.

In other preferred embodiments of the present invention an MRI imaging technique comprises a diffusion sequence so that a diffusion weighted MRI image of a subject can be

obtained. Diffusion weighted images are useful for, among other things, detection of ischemia, cytotoxic edema, and demyelinization in the brain. Diffusion weighted images of the brain are complicated because the brain pulsates and to observe diffusion a series of images of the brain taken at different times are compared. Generally, very fast imaging techniques such as EPI are used in diffusion studies of the brain. Data acquisition for such imaging, with updating of a primary transform using a diffusion sensitive EPI sequence, in accordance with a preferred embodiment of the present invention can be useful in improving the quality of diffusion sensitive MRI imaging of the brain and other pulsating and moving organs.

There is therefore provided in accordance with a preferred embodiment of the present invention a method for producing images of an object by MRI imaging comprising: acquiring a first set of data for the object at a first raster of coordinate points, in a first region in a k-space, using a first MRI imaging sequence; acquiring a second set of data for the object at a second raster of coordinate points in a second region in k-space using a second MRI imaging sequence, wherein the second region in k-space is included in the extent of the first region in k-space; using data from the second set of data to replace data from the first set of data thereby to produce a third set of data; and constructing a real space image of the object from the third set of data.

Preferably the real space image has substantially the same spatial resolution as a real space image constructed from the first set of data. The second region in k-space preferably includes the origin of k-space. Preferably, the first region in k-space includes the origin of k-space.

The second region in k-space is preferably significantly smaller than the first region in k-space. Preferably, the ratio of the size of the second region in k-space to the size of the first region in k-space is substantially equal to $R^n/(L-\Delta L)^n$, where R is the resolution of an image of the object constructed from the first set of data, L^3 is substantially equal to the volume in real space of a feature observed in the object and a change in the volume of the feature observed is substantially equal to $[L^n - (L-\Delta L)^n]$, and wherein n is equal to 2 and 3 for two dimensional and three dimensional imaging respectively.

In some preferred embodiments of the invention data in the third set of data is smoothed to remove discontinuities.

Preferably the time it takes to acquire the second set of data is substantially less than the time it takes to acquire the first set of data.

The magnetic field strengths used in the first and second MRI imaging sequences are preferably within established medical safety guidelines. Preferably, the time derivatives of the magnetic fields used in the first and second MRI imaging sequences are within established medical safety guidelines. The second MRI imaging sequence preferably, uses substantially the same magnetic gradient field strengths as the first MRI imaging method. Preferably, the time derivatives of the magnetic fields used in the first and second MRI imaging sequences are substantially the same. Preferably, the second method uses substantially the same receiver bandwidth as the first MRI imaging sequence.

In some preferred embodiments of the invention the first MRI imaging sequence is a gradient echo (GE) sequence or a spin echo (SE) sequence. The second MRI imaging sequence, in some preferred embodiments of the invention, is an EPI MRI imaging sequence.

In some preferred embodiments of the invention the second MRI imaging sequence is T_2 sensitive, in some others the second MRI imaging sequence is T_2^* sensitive.

In some preferred embodiments of the present invention the imaging is diffusion weighted.

Some MRI imaging methods in accordance with the present invention are sensitive to motion of parts of the body such as cardiac contractility, peristalsis, and respiratory motion.

In some preferred embodiments of the invention the MRI imaging method is sensitive to physiological changes such as those resulting from neural activity, blood flow or the absorption of substance by different tissues in the body.

In some preferred embodiments of the present invention, data in the first set of data that is not replaced is data that has remained substantially unchanged during the elapsed time between the acquisition of the first set of data and the acquisition of the second set of data and data that is replaced is data that has substantially changed during the elapsed time. Alternatively, or additionally, data in the first set of data that is replaced is data that defines larger features in the object and data that is not replaced is data that defines details of these features.

BRIEF DESCRIPTION OF FIGURES

The invention will be more clearly understood by reference to the following description of preferred embodiments thereof in conjunction with the figures, wherein common elements which appear in the figures are labeled with the same numeral, and in which:

Figs. 1A and 1B show respectively, a conventional planar echo imaging sequence (EPI) and a raster of points in k-space at which the sequence samples data for a k-transform of an object;

Fig. 2 is a schematic of a hybrid two dimensional MRI imaging technique, in accordance with a preferred embodiment of the present invention, for the rapid production of a sequence of real time two dimensional images of an object; and

Figs. 3A-3D schematically illustrate elements of a hybrid imaging process for the rapid production of a sequence of real time three dimensional images of an object in accordance with a preferred embodiment of the present invention.

DETAILED DESCRIPTION OF PREFERRED EMBODIMENTS

A simple formula can be used to relate important parameters of MRI imaging sequences and clarify their significance to preferred embodiments of the present invention.

The relationship $KR \cong 1$ used above, can be written, $\gamma G T_A R \cong 1$, since $K = \gamma G T_A$, where γ is the gyromagnetic ratio of the imaging nucleus, G the magnetic read gradient, and T_A the data acquisition time in the MRI imaging sequence. Resolution R may also be written as the field of view of the image, FOV, divided by the number of pixels in the MRI image. Then $KR = \gamma G T_A \, FOV/N = \gamma G T_D \, FOV = \gamma G(1/(2BW)) \, FOV \cong 1$, where T_D is the dwell time per point in k-space at which $S(\vec{k})$ is evaluated ($T_D = T_A/N$, since the number of pixels in the real space image equals the number of data points taken in k-space), and BW is the bandwidth of the receiver ($=1/(2T_D)$).

Consider a conventional GE or SE sequence and assume that the imaging nucleus is the water proton, that a slice having an area 20cm x 20cm is imaged, and that the image has 256 x 256 pixels (*i.e.* R = 0.8 mm). Then $\gamma = 4257$ Hz/gauss, FOV = 20, N = 256, and $GT_D \cong 11.75 \times 10^{-6}$. Assuming that a typical read time (i.e. T_A) for the GE or SE sequences is 3.072msec for a read line in k-space with 256 points, then $T_D = 12$ μsec, and $G \cong 0.98$ gauss/cm = 9.8 mT/m. The net dwell time for all 256 x 256 points in k-space at which data is taken for the slice is about 1 second. However, the total image acquisition time, T_I, is equal to $256T_R$, (for the case where each repetition of the sequence accumulates one read line of data) which is considerably longer than the total dwell time if T_R is on the order of T_1. For brain white matter for example, T_1 is about 0.5 sec, which would lead to a total image time T_I, for a single slice of brain tissue, using conventional GE and SE sequences, of approximately two minutes. The resolution of the GE and SE sequences might be acceptable for most real time imaging but the imaging time is too long. Not only is the total image time T_I much too long for rapid imaging of important physiological processes, but even the net dwell time is too long (*e.g.* it's too long to image a heart beat).

In comparison, consider an EPI sequence that acquires data at all 256 x256 data points in k-space for the slice in a single sequence, and that the imaging time is an acceptable, 100 msec. For this case the dwell time becomes 1.5μsec, the gradient G becomes 78.4mT/m, and the time rate of change of the read gradient field is on the order of 64 times that used in the GE and SE sequences discussed in the previous example. This time rate of change of field is large and potentially harmful to biological tissue.

In addition, whereas in the case of the SE and GE sequences receiver bandwidth is ≅ 42kHz, for the EPI sequence it is 336kHz. Therefore, although the EPI sequence can perform fast enough, it has serious technical handicaps, and as noted above, it does not generally have the resolution required.

Now consider using fast EPI to update only the central 64 x 64 k-space data points for the slice, in accordance with a preferred embodiment of the present invention. Assume a total net dwell time of 50msec. Then T_D is again 12μsec and bandwidth is ≅ 42kHz. Using the relationship $\gamma G T_D$ FOV ≅ 1, G has the value 9.8 mT/m, the same value used by the GE and SE sequences. Rise and fall times of the gradient field can be an acceptable 100 to 150μsec for read field gradient blips in the EPI sequence (see Fig. 2A). Such rise and fall times extend the acquisition time of the 64x64 data points from the net dwell time of 50msec to between 60 and 70msec.

It is therefore seen that a hybrid imaging process in accordance with a preferred embodiment of the present invention, that preferably uses a GE or SE imaging sequence to acquire a high resolution primary k-transform of an object imaged and a fast EPI imaging sequence to update part of the primary k-transform can produce real space images of the object with substantially the rapidity of the fast EPI sequence and substantially the resolution of the high resolution GE or SE sequence. It is also seen that the hybrid imaging process in accordance with the present invention can do this with conventional gradient strengths and receiver bandwidths, *i.e.* with conventional GE or SE equipment.

The imaging sequences used in a hybrid imaging sequence in accordance with a preferred embodiment of the present invention can be tailored to a type of image and type of image contrast desired. For example, for diffusion imaging of the brain a diffusion pulse train can be added to the imaging sequence and preferably updated with snapshot EPI techniques. In some preferred embodiments of the invention the sequence provides T_2 contrast. In other preferred embodiments the sequence provides T_2^* contrast. Other preferred embodiments of the present invention can be made sensitive to temporal changes in the body in order to image

peristalsis or cardiac contractility, or physiological changes resulting from neural activity. Still other preferred embodiment can be tailored for use with contrast agents such as Gd-DTPA or for imaging changes in tissues due to oxygen uptake.

Fig. 2 shows, schematically, a two dimensional MRI hybrid imaging process 60, in accordance with a preferred embodiment of the present invention, for rapid sequential updating of MRI images in a real time study of an object.

A primary two dimensional k-transform, $S_0(k_x,k_y)$, of the object is acquired at a time t_0, over a primary raster 62, of points 64, in k-space. Preferably, primary raster 62 comprises 256 equally spaced read lines 66, having 256 equally spaced read points each. Preferably, the perimeter of primary raster 62 is a square 67, whose center is at the origin of k-space. $S_0(k_x,k_y)$ is calibrated and phase corrected using methods known in the art so that the k-space origin is correctly centered. A primary image IM_0 of the object is constructed by Fourier transforming primary k-transform $S_0(k_x,k_y)$.

Primary k-transform $S_0(k_x,k_y)$ is preferably acquired using a high resolution MRI imaging sequence such as preferably, a GE or SE sequence of the type shown in Figs. 1A and 1C respectively.

Phase correction of the primary k-transform should not be required if a SE sequence is used. However if a GE technique is used, phase correction can preferably be carried by acquiring calibration data for $S_0(k_x,k_y)$ at read points along a single k_x read line without phase encoding along k_y. The calibration data is Fourier transformed and the phase of each pixel along the x axis calculated. A complete set of data for $S_0(k_x,k_y)$ is then acquired and Fourier transformed for the k_x variable only, to get an interim function $IF(x,k_y)$. Interim function $IF(x,k_y)$ is a function of the real space variable x and the k-space variable k_y. The phases calculated from the calibration read line are complex subtracted for each pixel, point by point, for every read line of the function $IF(x,k_y)$. and the phase corrected $IF(x,k_y)$ is Fourier transformed for the k_y variable to get a phase corrected primary image IM_0. Primary image IM_0 is then Fourier transformed back into k-space to yield a primary k-transform.

At a subsequent time, t_1, an update k-transform, $S_u(k_x,k_y)$, of the object is acquired at an update raster 68, of read points 70. Preferably, update raster 68 comprises 64 read lines 72, having 64 equally spaced read points each. Preferably, the spacing between read lines 72 and read points 70 in update raster 68 are the same as the spacing between read lines 66 and read points 64 in primary raster 62. Preferably, the perimeter 69, of update raster 68 is a square whose center is at the origin of k-space. The area of update raster 68 is therefore congruent with a central square area 74, of primary raster 62. which is 64 read lines high by 64 read

points wide and read points in raster 68 are congruent with read points 64 in central area 74. Like $S_0(k_x,k_y)$, update k-transform $S_u(k_x,k_y)$ is calibrated and phase corrected using methods known in the art so that the k-space origin is correctly centered.

Values of $S_0(k_x,k_y)$, at read points 64 in central area 74 of primary raster 62 are then replaced with values calculated from update image $S_u(k_x,k_y)$ to produce a new k-transform of the object. The new k-transform is Fourier transformed to produce an updated image, IM1, of the object at time t1. The process is repeated again at a time t2, and subsequently as many times as needed and conditions allow. The time between images can be as short as the update time, which is on the order of from 20-100msec, if not limited by other parameters such as T_1 recovery time.

Prior to replacement, amplitudes of $S_u(k_x,k_y)$ are calibrated to amplitudes of $S_0(k_x,k_y)$. If there is a mismatch between the spacing of read lines and read points in update raster 68 and central area 74 of raster 62 then measured values of $S_u(k_x,k_y)$ are used to interpolate appropriate values of $S_u(k_x,k_y)$ to replace values of $S_0(k_x,k_y)$.

Preferably, read points 70 along the inside edge of the area of update raster 68 fall within an area of primary raster 62 where the k-transform of the object does not change significantly during the real time study of the object. This facilitates the calibration of amplitudes between $S_u(k_x,k_y)$ and $S_0(k_x,k_y)$ and the interpolation of values of $S_u(k_x,k_y)$ when necessary in the case where read lines between primary raster 62 and update raster 68 get misaligned. Aspects of matching data and smoothing of transitions at the boundaries between two sets of related k-transform data are discussed in a patent application titled, "Removing Discontinuities in MRI K-Space Data", filed in the US Patent Office by a same applicant as an applicant of this application, on September 14, 1998, the disclosure of which is incorporated herein by reference.

It should be realized that the full primary image can be updated as needed or desired. An indication as to when this is required can be inferred from the quality of the images constructed from the updated k-transforms.

Three dimensional hybrid imaging processes for rapid sequential imaging, in accordance with a preferred embodiment of the present invention, are based on the same principles as the two dimensional processes described above.

Figs. 3A-3D illustrate elements of a three dimensional hybrid imaging process for imaging a thick slice of an object in accordance with a preferred embodiment of the present invention.

A high resolution three dimensional primary k-transform $S_0(k_x,k_y,k_z)$ of the object is acquired at read points in a primary three dimensional raster in k-space. Preferably, the acquisition is made using a three dimensional GE imaging sequence 80 of the type shown in Fig. 3A. In imaging sequence 80 a broad band selection RF pulse 82 and selection gradient 84 select a thick slice of the object for imaging. Phase encoding is done in both the y and z directions using y phase gradient 88 and z phase gradient 90 respectively. Y phase gradient 88 is step increased by a fixed y phase increment 89 for each read line scanned and z phase gradient 90 is step increased by a fixed z phase increment 91 after all the lines in a read plane are scanned. Step increases for the y and z phases are performed between repetitions of GE sequence 80. Data is acquired during x read gradient 92 by sampling data echo 96. Gradient 94 which precedes read gradient 92initializes the starting k_x value for each read line and centers data echo pulse 96 at the center of read gradient 92.

Preferably, the raster of read points at which $S_0(k_x,k_y,k_z)$ is evaluated comprises L x N x M read points in k-space. Preferably the read points are distributed on L identical parallel plane surfaces equally spaced along the z axis, each plane surface having preferably the same number N x M read points. Preferably, the N x M read points in a plane lie on N read lines of M read points each, parallel to the k_x axis. Preferably, the distance between adjacent read lines on a plane is the same for all read lines. The distance between a read point and an adjacent read point on a same read line is preferably the same for any read point in the raster.

Reference is now made to Fig. 3B. Preferably, the L plane surfaces of the primary raster (not shown) are contained in a primary k-volume 100 which is rectangular and centered on the k-space origin.

Following the acquisition of the primary k-transform, three dimensional update k-transforms, $S_u(k_x,k_y,k_z)$, are preferably evaluated at a reduced number of read points (not shown) in a rectangular update k-volume 102 contained inside primary k-volume 100. Update k-volume 102 is preferably centered on the origin of k-space and much smaller than primary k-volume 100.

As in the two dimensional case, data from the three dimensional update k-transform $S_u(k_x,k_y,k_z)$ replaces data in the three dimensional primary k-transform $S_0(k_x,k_y,k_z)$ in order to sequentially image the observed object in real time. The relative size of the update k-volume to the primary k-volume (which is generally the ratio of the number of data points in the update k-transform to the number of data points in the primary k-transform) is preferably, substantially equal to $R^3/(L-\Delta L)^3$ where R is the resolution of the real space images L is the characteristic

size of the features in the object observed and ΔL is the characteristic size of the changes in these features.

Again, as in the two dimensional case, the reduced number of data points required for a three dimensional update makes the use of very fast three dimensional MRI imaging sequences, such as three dimensional EPI, advantageous. As a result, updates can be made very rapidly and MRI imaging procedures, in accordance with a preferred embodiment of the present invention, can provide rapid three dimensional real time sequential imaging with high resolution.

A three dimensional EPI sequence 136, preferably used for accumulating data for update k-transforms is shown in Fig. 3C. For clarity and ease of exposition, EPI sequence 120 refers to an update volume enclosing a raster of 4 x 4 x 4 read points, *i.e.* 4 read planes (L=4) having 4 read lines (N=4) with each read line having 4 read points (M=4).

Following a selection pulse 122, with a flip angle α, a read gradient blip train 124 comprising 16 read blips 126 is applied to the x axis. A phase gradient blip train 128 comprising 12 phase blips 130 is applied to the y axis and a phase gradient blip train 132 comprising 3 phase blips 134 is applied to the z axis. Blip trains 124, 128 and 132, begin with negative initialization gradients 136, 138 and 140 respectively, which initialize the coordinates of the starting read point of the data scan.

Since there are 16 read lines in the raster, and all the read points on a read line are read during one read gradient blip 126, there are 16 read gradient blips 126 in read gradient blip train 124. Each read blip is lasts for a time T_M. All except every fourth read gradient blip 126 in blip train 124 is followed with a y phase gradient blip 130 which is centered at the zero crossing point between read blips 126. Each y phase gradient blip 130 lasts for a time T_Y, and increases k_y by $\gamma G_y T_y$, thereby advancing the k-scan to the next read line in the read plane. Every fourth read gradient blip 126 is followed by a z phase gradient blip134 which lasts for a time T_Z and increases k_z by $\gamma G_z T_z$ to advance the k-scan to the next read plane. Z phase gradient blips 134, when they occur, like y phase gradient blips 130, are centered on the zero crossover points between read blips 126. Y phase gradient blips 130 change sign following each z phase gradient blip 134 because from one read plane to the next, the direction of the k-scan reverses in the y direction. Data is recorded from a train 140, of echo pulses comprising data echo pulses 142. There is an echo pulse for each read gradient blip 126. The maximum amplitude echo pulse generally occurs at the origin of k-space unless the echoes have been significantly reduced by transverse T_2 or T_2^* dephasing.

Total data acquisition time T_A for an update volume using an EPI scan of this type is equal to $NxLxT_M$. With an amplitude of about 9.8 mT/m and rise time of 116μsec for read gradient blips 139, then for a read line having 16 read points and dwell time of 12μsec per read point T_M = 424μsec. Data for a complete update raster of 16x16x16 read points is then acquired in $256T_M$= 108msec.

Fig. 3D shows a k-space trajectory 154, traversed by 3 dimensional EPI sequence 120 as it samples data at 4x4x4 read points 156, in an update raster 154. Raster 154 comprises 4 read planes 158 separated by a distance in k-space equal to $\gamma G_Z T_Z$, where γ is the gyromagnetic ratio of the imaging nucleus, G_Z is the amplitude of z phase blips 143 and T_Z is the duration of phase blips 143. The relative displacement of the read planes along the z axis is noted by the numeral at the lower right of the read plane. Read plane 158 labeled with "0" coincides with the k_xk_y plane, read plane 158 labeled "-1" is displaced along the negative k_Z axis by $\gamma G_Z T_Z$. Each read plane 158 has 4 read lines 160 of length $\gamma G_X T_M$ separated by $\gamma G_y T_y$, where G_X, T_M, G_y, and, and T_y are the gradient blip amplitudes and times of read gradient blips 139 and phase blips 141 respectively. The data scan starts at read point 162 and proceeds along trajectory 152 in the direction of arrows 164.

Similarly to the two dimensional case, for three dimensional rapid sequential imaging of an object, in accordance with a preferred embodiment of the present invention, spacing between read planes, read lines and read points in an update raster are preferably identical to spacing between read planes, read lines, and read points in the primary raster for which the update is intended. Preferably, the update raster includes read points in k-space for which the values of a primary k-transform of the object do not change much. This facilitates calibrating update k-transform data to the primary k-transform data and smoothing transitions between update data and data retained from the primary k-transform that is used for imaging at times subsequent to the time when the primary k-transform is acquired.

It should be realized that update rasters do not necessarily have to occupy the same volume of k-space for each update. As changes in an object imaged accumulate over time, data that was initially sufficiently accurate to be retained from a primary k-transform of the object and used for imaging at one time, might degrade at a later time to such an extent that it should be replaced. In such cases the volume of a raster of read points might be enlarged or moved or otherwise altered to satisfy and anticipate needs.

The present invention has been described using a non limiting detailed description of a preferred embodiment thereof. Variations of the embodiment described will occur to persons

of the art. The detailed description is provided by way of example and is not meant to limit the scope of the invention which is limited only by the following claims:

CLAIMS

1. A method for producing images of an object by MRI imaging comprising:

acquiring a first set of data for the object at a first raster of coordinate points, in a first region in a k-space, using a first MRI imaging sequence;

acquiring a second set of data for the object at a second raster of coordinate points in a second region in k-space using a second MRI imaging sequence, wherein the second region in k-space is included in the extent of the first region in k-space;

using data from the second set of data to replace data from the first set of data thereby to produce a third set of data; and

constructing a real space image of the object from the third set of data.

2. A method according to claim 1 wherein the real space image has substantially the same spatial resolution as a real space image constructed from the first set of data.

3. A method according to claim 1or claim 2 wherein the second region in k-space includes the origin of k-space.

4. A method according to any of the preceding claims wherein the first region in k-space includes the origin of k-space.

5. A method according to any of the preceding claims wherein the second region in k-space is significantly smaller than the first region in k-space.

6. A method according to claim 2 wherein the ratio of the size of the second region in k-space to the size of the first region in k-space is substantially equal to $R^n/(L-\Delta L)^n$, where R is the resolution of an image of the object constructed from the first set of data, L^3 is substantially equal to the volume in real space of a feature observed in the object and a change in the volume of the feature observed is substantially equal to $[L^n - (L-\Delta L)^n]$, and wherein n is equal to 2 and 3 for two dimensional and three dimensional imaging respectively.

7. A method according to any of the preceding claims wherein data in the third set of data is smoothed to remove discontinuities.

8. A method according to any of the preceding claims wherein the time it takes to acquire the second set of data is substantially less than the time it takes to acquire the first set of data.

9. A method according to any of the preceding claims wherein the magnetic field strengths used in the first and second MRI imaging sequences are within established medical safety guidelines.

10. A method according to any of the preceding claims wherein the time derivatives of the magnetic fields used in the first and second MRI imaging sequences are within established medical safety guidelines.

11. A method according to any of the preceding claims wherein the second MRI imaging sequence uses substantially the same magnetic gradient field strengths as the first MRI imaging method.

12. A method according to any of the preceding claims wherein the time derivatives of the magnetic fields used in the first and second MRI imaging sequences are substantially the same.

13. A method according to any of the preceding claims wherein the second method uses substantially the same receiver bandwidth as the first MRI imaging sequence.

14. A method according to any of the preceding claims wherein the first MRI imaging sequence is a gradient echo (GE) sequence.

15. A method according to any of claims 1-13 wherein the first MRI imaging sequence is a spin echo (SE) sequence.

16. A method according to any of the preceding claims wherein the second MRI imaging sequence is an EPI MRI imaging sequence.

17. A method according to any of the preceding claims wherein the second MRI imaging sequence is T_2 sensitive.

18. A method according to any of the preceding claims wherein the second MRI imaging sequence is T_2^* sensitive.

19. A method according to any of the preceding claims wherein the imaging is diffusion weighted.

20. A method according to any of the preceding claims wherein the imaging is sensitive to motion of parts of the body such as cardiac contractility, peristalsis, and respiratory motion.

21. A method according to any of the preceding claims wherein the imaging is sensitive to physiological changes such as those resulting from neural activity, blood flow or the absorption of substances by different tissues in the body.

22. A method according to any of the preceding claims wherein data in the first set of data that is not replaced is data that has remained substantially unchanged during the elapsed time between the acquisition of the first set of data and the acquisition of the second set of data and data that is replaced is data that has substantially changed during the elapsed time.

23. A method according to any of the preceding claims wherein data in the first set of data that is replaced is data that defines larger features in the object and data that is not replaced is data that defines details of these features.

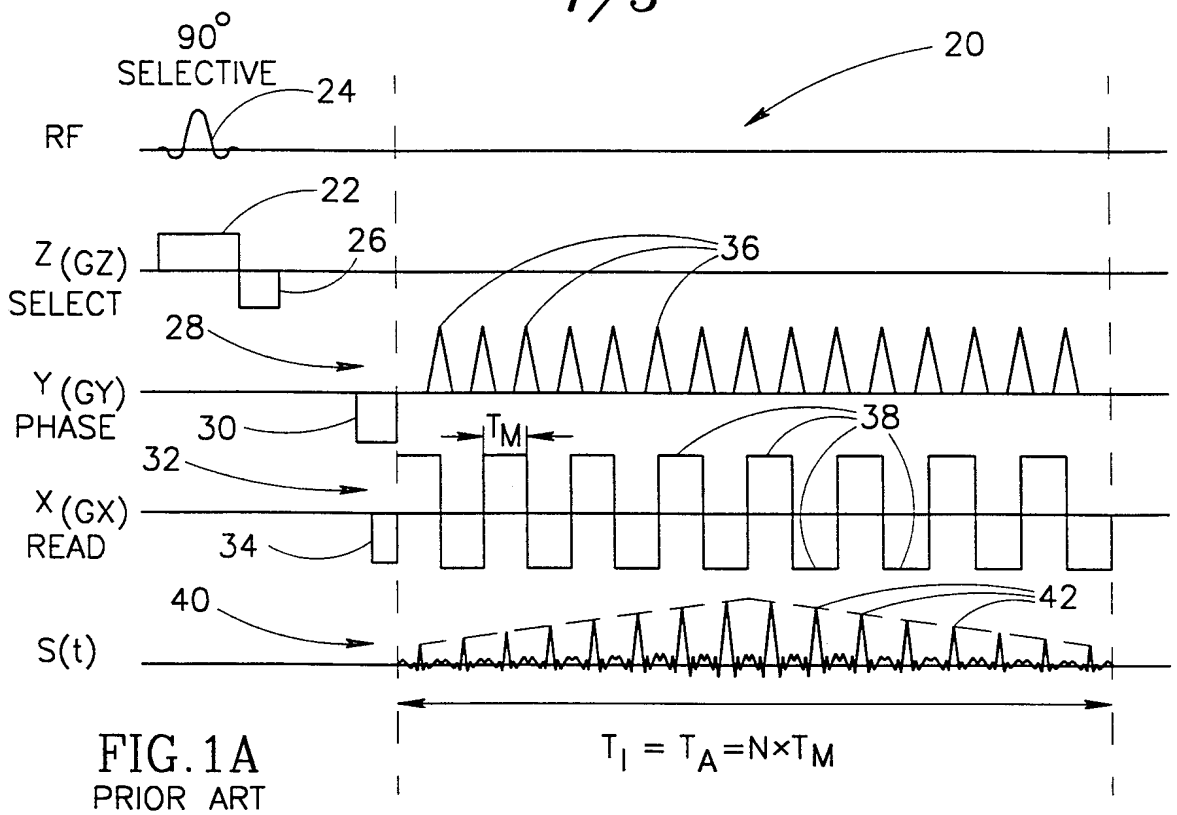

FIG. 1A
PRIOR ART

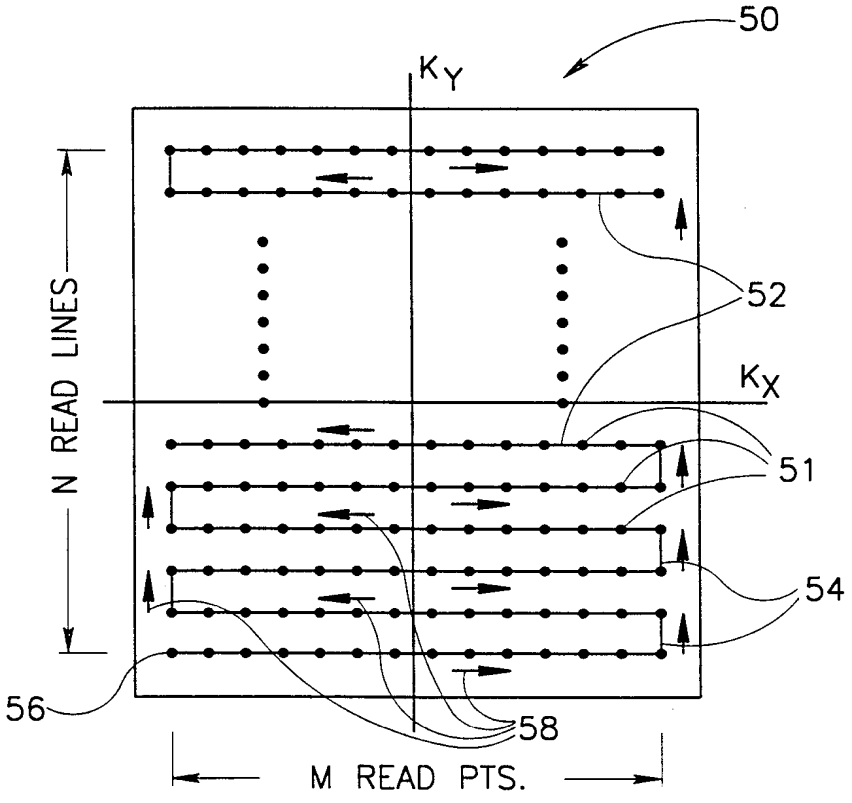

FIG. 1B
PRIOR ART

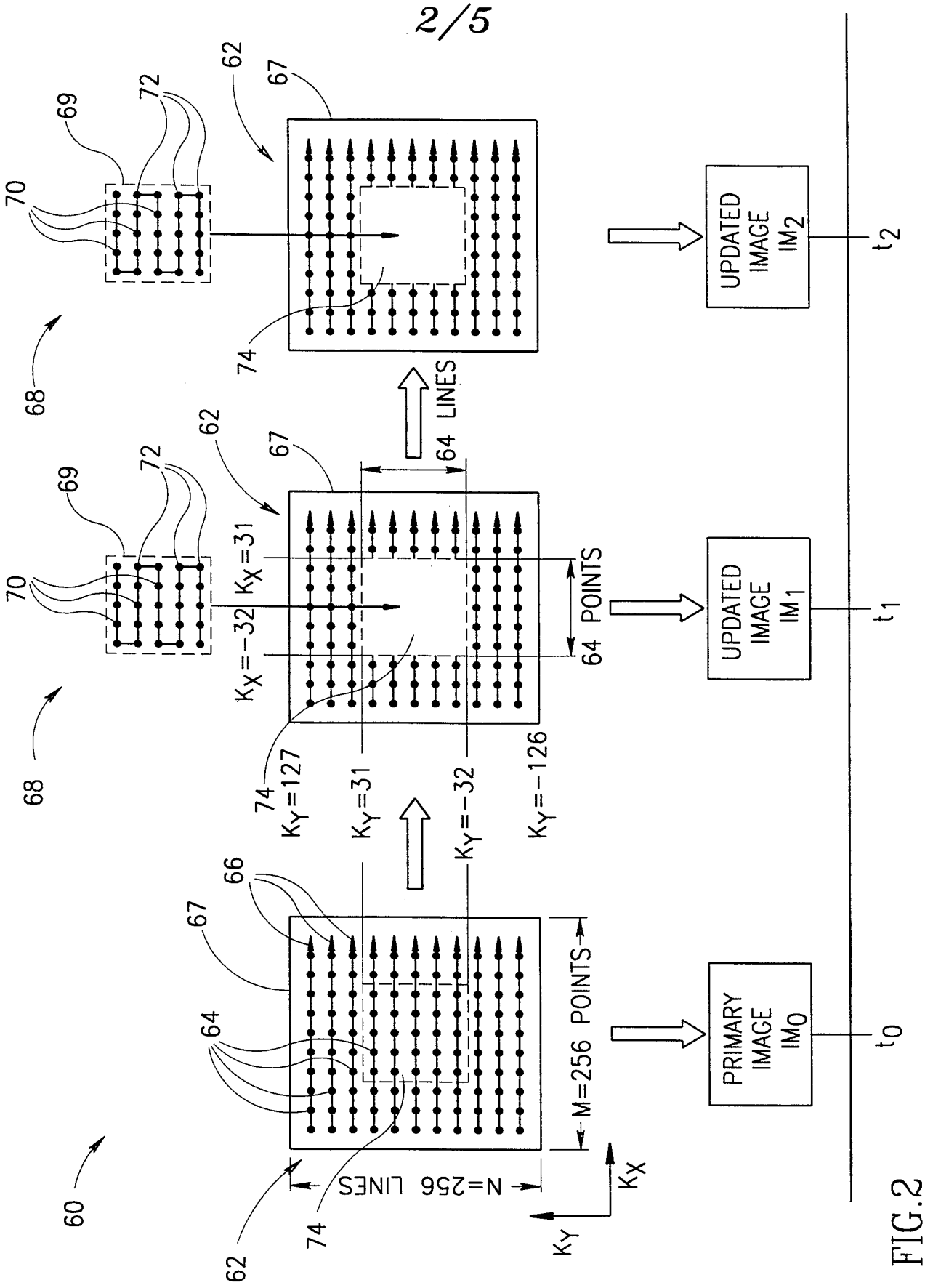
60
62
64
66
67
68
69
70
72
74
N=256 LINES
M=256 POINTS
64 LINES
64 POINTS
K_X
K_Y
$K_X=31$
$K_X=-32$
$K_Y=127$
$K_Y=31$
$K_Y=-32$
$K_Y=-126$
PRIMARY IMAGE IM_0
UPDATED IMAGE IM_1
UPDATED IMAGE IM_2
t_0
t_1
t_2

FIG.2

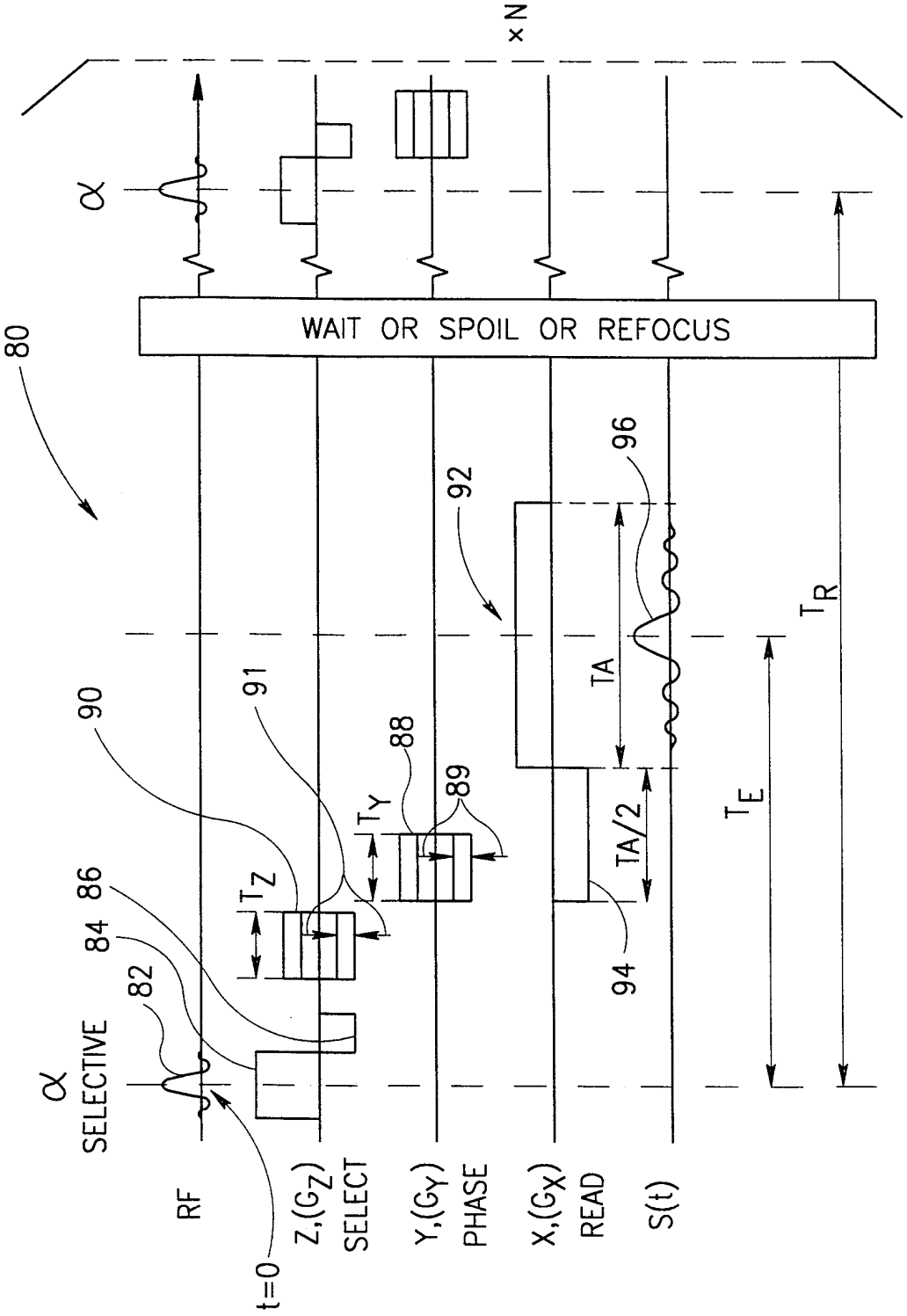

FIG.3A
PRIOR ART

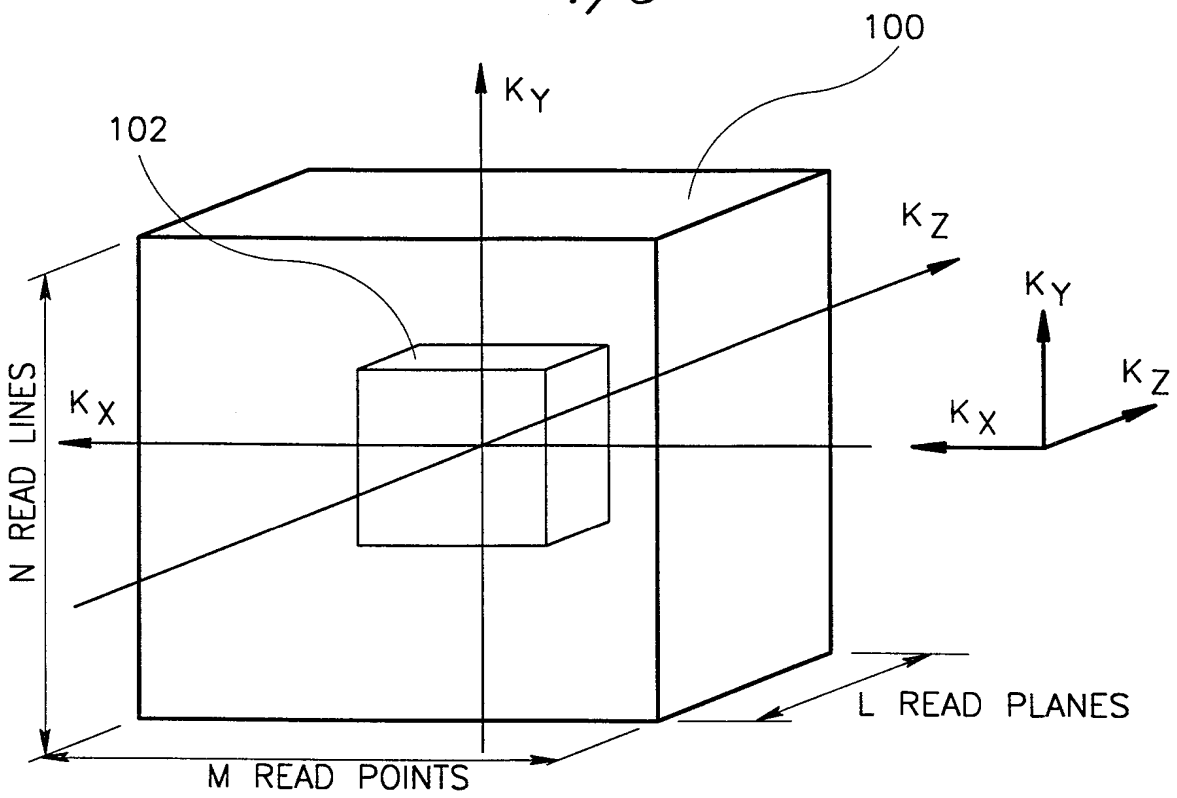

FIG.3B

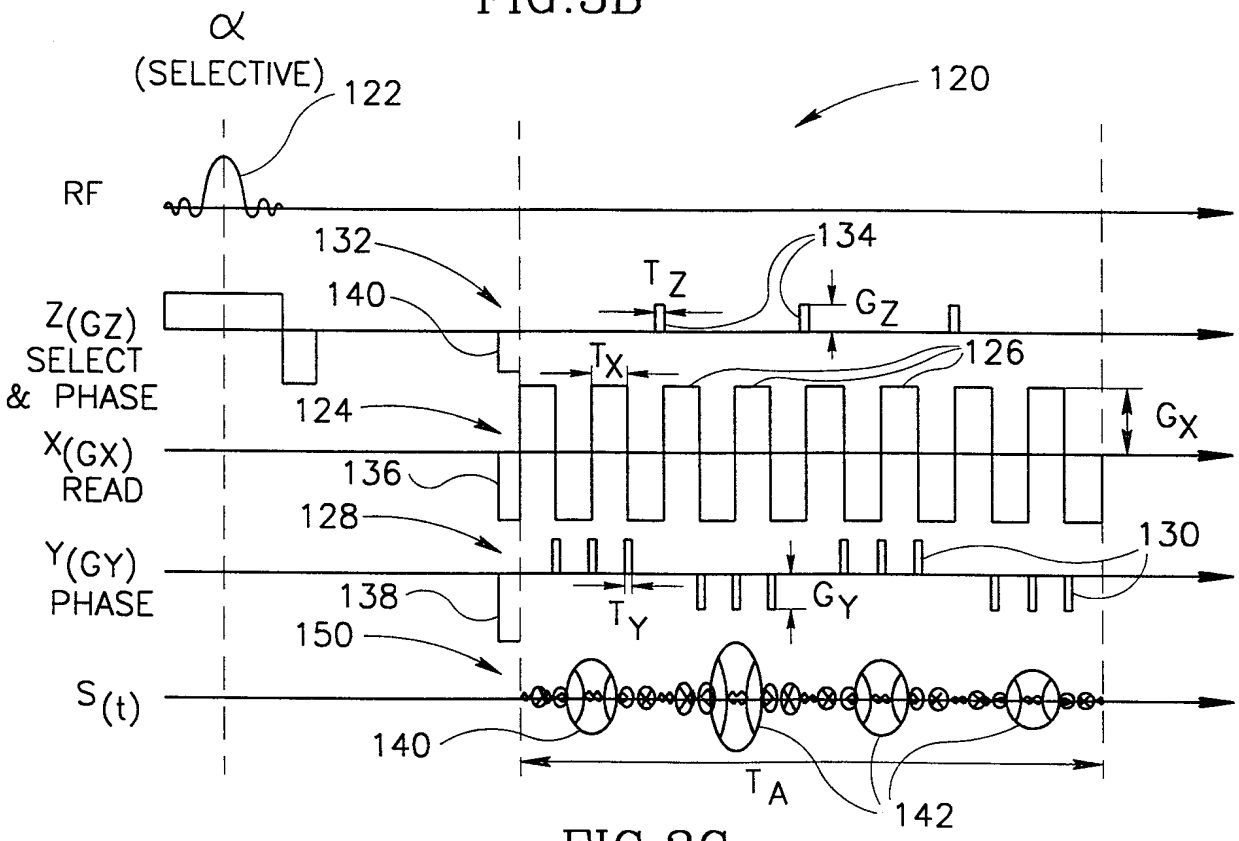

FIG.3C
PRIOR ART

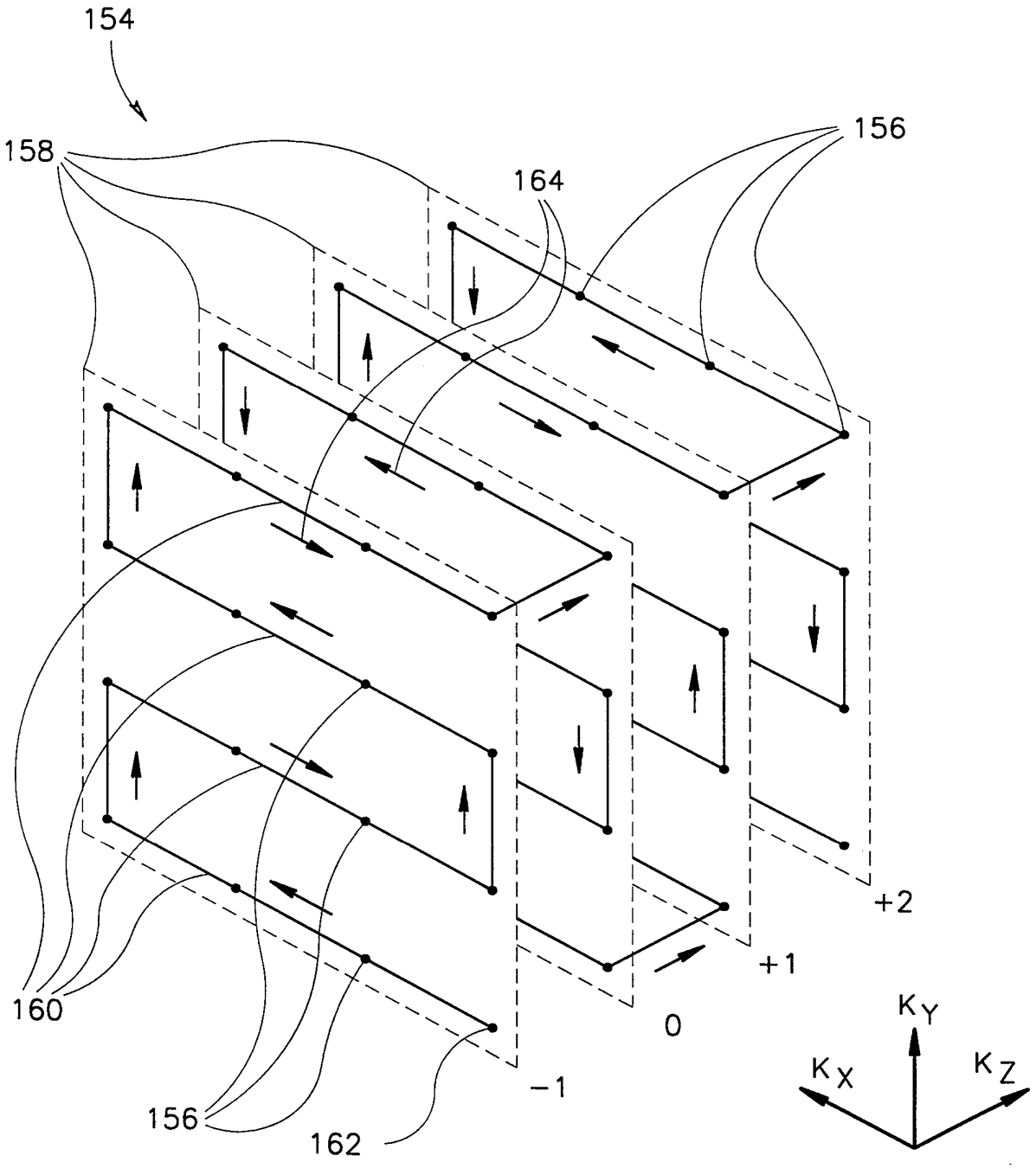

FIG.3D
PRIOR ART

INTERNATIONAL SEARCH REPORT

International Application No
PCT/IL 98/00446

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 G01R33/561

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 G01R

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 543 468 A (KONINKL PHILIPS ELECTRONICS NV) 26 May 1993 see abstract and see column 5, line 51 - column 10, line 18; figures 2-4 ---	1-23
X	J.J.VAN VAALS ET AL.: ""Keyhole" Method for Accelerating Imaging of Contrast Agent Uptake" JOURNAL OF MAGNETIC RESONANCE IMAGING (JMRI), vol. 3, 1993, pages 671-675, XP002089527 see the whole document --- -/--	1-6,8-23

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
11 January 1999	29/01/1999

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Lersch, W

2

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International Application No
PCT/IL 98/00446

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
X	JIA-HONG GAO ET AL: "IMPROVING THE TEMPORAL RESOLUTION OF FUNCTIONAL MR IMAGING USING KEYHOLE TECHNIQUES" MAGNETIC RESONANCE IN MEDICINE, vol. 35, no. 6, 1 June 1996, pages 854-860, XP000594136 see the whole document	1-23
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2

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